Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1 and 3-9 are pending in the application, with 1 being the independent claim. Claim 1 is sought to be amended. Support for the amendment to claim 1 is found in the specification at page 3, lines 5-6. New claims 8 and 9 are sought to be added. Support for new claims 8 and 9 is found in claim 1 as originally filed. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1, 3, and 7 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Mandecki (U.S. Patent No. 6,046,003) in view of Akram *et al.* (U.S. Patent No. 6,250,192). (Office Action, page 2). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Mandecki teaches a method for producing a labeled nucleic acid (e.g., fluorescently-labeled target DNA bound to probe attached to the surface of the transponder), wherein the method comprises binding the nucleic acid (e.g., oligonucleotides) to a large scale integrated circuit (e.g., solid phase particles having a transponder associated with each particle), and recording specific information (e.g., the sequence of the oligonucleotide) on the large scale integrated circuit (column 1, lines 55-column 2, line 6, column 17, lines 28-44). . . .

> Mandecki does not teach the use of integrated circuits with 320 million bits of memory (equivalent to 40 million bytes or 40 megabytes of memory).
>
> Akram teaches the use of RFID integrated circuits with a capacity of 64 megabytes (see column 2, lines 1-15, especially line 9.
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the Mandecki device to use large integrated circuits since Mandecki expressly notes "The present invention can be practiced with different transponders, which might be of different dimensions and have different electronic memory capacity (see column 5, lines 57-60).

(Office Action, pages 2-3). Applicants respectfully disagree.

The claims as amended are directed to a method for producing a labeled nucleic acid or protein, comprising binding the nucleic acid or protein to a LSI that comprises more than 320 million bits of memory, wherein the nucleic acid is double-stranded or circular, and wherein specific information characteristic to the nucleic acid or protein is recorded on the LSI.

In contrast, Mandecki describes a method for determining the sequence of target nucleic acids in which oligonucleotide probes attached to transponders are allowed to interact with the target nucleic acids and the binding between the probes and the targets is detected (sequencing by hybridization). This method requires hybridization between the probes and the target nucleic acids. Thus, the probes immobilized on the transponders must be in a form suitable for hybridization. Mandecki states that "[i]t is preferred that the immobilized nucleic acids are single-stranded (col. 3, lines 27-29). Throughout the patent, Mandecki refers only to the use of oligonucleotides as probes (*e.g.*, col. 3, lines 36-54; col. 4, line 67 to col. 5, line 2; col. 7, lines 52-56;) and fails to describe or exemplify any other embodiments.

Given that (i) the purpose of Mandecki's described method is to determine the sequence of target nucleic acids through a sequencing by hybridization method, (ii) probes used in the sequencing by hybridization method should be single-stranded, and (iii) Mandecki fails to teach how to carry out the described sequencing method with any probes other than single-stranded oligonucleotides, it could not have been obvious to one of ordinary skill in the art to modify the method of Mandecki to produce transponder-linked probes that are either double-stranded or circular. One would not have been motivated to modify Mandecki in this manner as one would expect double-stranded or circular probes to not work in the described sequencing method. Thus, Mandecki does not provide any teaching or motivation to bind a double-stranded or circular nucleic acid to a LSI.

Furthermore, the Examiner admits that Mandecki does not teach the use of integrated circuits with 320 million bits of memory. The Examiner does point out that Mandecki notes "the present invention can be practiced with different transponders, which might be of different dimensions and have different electronic memory capacity" (col. 5, lines 57-60). The Examiner asserts that Akram *et al.* teach the use of RFID (radio-frequency ID) integrated circuits with a capacity of 64 megabytes and that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the Mandecki device to use larger integrated circuits.

Applicants respectfully disagree. The invention of Akram *et al.* is related to methods for sawing semiconductor wafers. According to Akram *et al.*, each integrated circuit on a conventional wafer has the same size and rectangular configuration and is arranged in rows and columns. Thus, a typical wafer sawing method comprises cutting

the wafer along the mutually parallel and perpendicular streets between each discrete integrated circuit to cut out integrated circuits with an identical size (see col. 1, lines 44 to 67). In contrast to this conventional method, Akram *et al.* provide a method and apparatus for sawing semiconductor wafers having various integrated circuits and other semiconductor devices thereon, each of which may be of a different size (column 2, lines 1-4). As is clear from the above, Akram *et al.* only teach a method and apparatus for cutting out integrated circuit(s) from a semiconductor wafer (*i.e.*, a method for producing IC chips), and clearly fail to teach or suggest any particular application of thus-produced IC chips. Akram *et al.* is completely silent about the present invention's idea of applying an LSI to the labeling of nucleic acids or other biological macromolecules. Akram *et al.*'s methods and apparatus for sawing a semiconductor wafer (*i.e.*, methods for producing an LSI chip) represent a technology that is distinct from and has no direct relevance to the present invention, and thus, the Examiner's position that the combination of Akram *et al.* and Mandecki is *prima facie* obvious to one of ordinary skill in the art is not proper.

Furthermore, Akram *et al.* do not teach RFID integrated circuits with a capacity of 64 megabytes. The Examiner cites col. 2, lines 1-13 as a disclosure of an "RFID device with 64 megabytes." This interpretation of Akram *et al.* is incorrect. In col. 2, lines 1-4, Akram *et al.* state: "It may, however, be desirable to design and fabricate a semiconductor wafer having various integrated circuits and other semiconductor devices thereon, each of which may be of a different size." Akram *et al.* continue on to illustrate, as examples of situations where a semiconductor wafer having various integrated circuits or such with different sizes is desirable, the following two *independent* cases:

(i) "[I]n radio-frequency ID) (RFID) applications, a battery, chip and antenna could be incorporated into the same wafer such that all semiconductor devices of an RFID electronic device are fabricated from a single semiconductor wafer."

(ii) "[M]emory dice of different capacities, for example, 4, 16, and 64 megabyte DRAMs, might be fabricated on a single wafer to maximize the use of silicon `real estate' and reduce thiefage or waste of material near the periphery of the almost-circular (but for the flat) wafer."

As shown above, Akram *et al.* describe the "RFID device" and a memory dice with "64 megabytes" as entirely separate entities. The RFID application of (i) is an example of the case where fabricating a semiconductor wafer that has various semiconductor devices with different sizes (such as a battery, chip, and antenna) thereon is desirable because a complete RFID electronic device can be cut out from a single wafer. On the other hand, the wafer of (ii) including 4, 16, and "64 megabytes" DRAMs is an example where processing a wafer having various sizes of integrated circuits is desirable because, by appropriately placing the integrated circuits according to their size, a circular wafer can be efficiently used to its edge and waste of material near the periphery can be reduced. There is no description combining examples (i) and (ii) in Akram *et al.* In other words, Akram *et al.* do not describe an RFID device containing a DRAM of any size. Thus, even if one of ordinary skill in the art were to combine Mandecki and Akram *et al.*, one would not arrive at the present invention since Akram *et al.* do not teach at all an "RFID device with 64 megabytes."

The solid phase particles described by Mandecki requires a transponder, *i.e.*, a radiotransmitter-receiver (col. 5, lines 8-11). Mandecki provides no suggestion or

motivation to use a DRAM of any size as part of the solid phase particles, much less one of 64 megabytes. Thus, no suggestion or motivation can be found in either of the cited references to modify the teachings of Mandecki by incorporating the RFID or the DRAM described in Akram *et al.*

In the Advisory Action dated November 9, 2006, the Examiner stated, based on *DyStar v. Patrick Co.*, No. 06-1088, page 21 (Fed. Cir. 2006), that motivation to combine the two references exists even in the absence of any hint of suggestion in the references themselves, as a technology-independent improvement resulting in a product or process that is more desirable. Applicants respectfully assert that the *DyStar* situation does not exist here. Because Akram *et al.* do not teach an RFID device with 64 megabytes, modification of the product disclosed in Mandecki with the teachings of Akram *et al.* would not result in a product that is stronger, cheaper, faster, lighter, smaller, more durable, or more efficient. Therefore, there is no motivation based on technology-independent improvement.

It is respectfully requested that the rejection of claims 1, 3, and 7 over Mandecki in view of Akram *et al.* be withdrawn.

Claims 1, 3, 5, and 7 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nova *et al.* (U.S. Patent No. 5,741,462) in view of Akram *et al.* (Office Action, page 5). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Nova teaches a method for producing a labeled protein or gene (see abstract), wherein the method comprises binding the protein to a large scale integrated circuit (see column 29, line 45 to column 30, line 14, where antibodies are bound to the integrated circuit), and recording specific information that is characteristic of the peptide (see

> column 29, lines 50-55 where each antibody "is given a specific identification tag") on the large scale integrated circuit (see columns 29 and 30). . . .
>
> Nova does not teach the use of integrated circuits with 320 million bits of memory (equivalent to 40 million bytes or 40 megabytes of memory).
>
> Akram teaches the use of RFID integrated circuits with a capacity of 64 megabytes (see column 2, lines 1-15, especially line 9.
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the Nova device to use larger integrated circuits since Nova expressly notes "Based on current semiconductor integrated circuit fabrication process capabilities, in a preferred embodiment the finished chip on which all of the listed components are integrated is on the order of 1 mm.times.1 mm [.about.40 mils.times.40 mils], with a memory capacity of 1024 bits. Greater memory capacity, where needed, and smaller chips, however, will be preferred. The chip may be larger to accommodate more memory if desired, or may be smaller as design rules permit smaller transistor san higher device densities (see column 21, lines 8-16).

(Office Action, pages 5-6). Applicants respectfully disagree.

The Examiner admits that Nova *et al.* do not teach the use of integrated circuits with 320 million bits of memory. The Examiner does point out that Nova *et al.* note "[g]reater memory capacity, where needed, and smaller chips, however, will be preferred" and "[t]he chip may be larger to accommodate more memory if desired, or may be smaller as design rules permit smaller transistors and higher device densities" (col. 21, lines 8-16).

As discussed above, the methods and apparatus of Akram *et al.* relate to sawing silicon wafers and have no direct relevance to the present invention's method. Thus, Nova *et al.* and Akram *et al.* are not a proper basis for the finding of a *prima facie* case of obviousness. Furthermore, as discussed above, Akram *et al.* do not even teach an

"RFID device with 64 megabytes." Thus, even if one of ordinary skill in the art were to combine Nova *et al.* and Akram *et al.*, one would not arrive at the present invention since Akram *et al.* do not teach at all an "RFID device with 64 megabytes."

Moreover, Nova *et al.* disclose integrated circuits comprising 1024 bits as a preferred embodiment (column 21, lines 8-16). Nova *et al.* further state that "[i]nformation to be written into the memory need not be detailed since the data stored in the memory is primarily acting as an identification marker that is traceable to a more detailed record stored in the host computer memory" (column 21, lines 60-63). These disclosures indicate that Nova *et al.* did not contemplate the use of high capacity memory in the disclosed devices because only small amounts of information would need to be stored for each molecule. Despite the statement in Nova *et al.* that greater memory capacity can be used, there is no teaching or suggestion in Nova *et al.* to use large scale integrated circuits such as the 320 million bits of memory required in the presently claimed invention.

It is respectfully requested that the rejection of claims 1, 3, 5, and 7 over Nova *et al.* in view of Akram *et al.* be withdrawn.

Claim 4 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Mandecki in view of Akram *et al.* and further in view of Stavrianopoulos *et al.* (U.S. Patent No. 4,994,373). (Office Action, page 7). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Mandecki in view of Akram teach the limitations of claims 1, 3 and 7 as discussed above.
>
> Mandecki does not teach the specific substrates of claim 4.

> Stavrianopoulos teaches attachment of nucleic acids to plastic matrices (see column 12, lines 5-15, for example).
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the epoxy resin of Stavrianopoulos to attach the nucleic acids of Mandecki in view of Akram since Stavrianopoulos notes "An improved capability for fixing or immobilization of DNA to non-porous siliceous solid supports, such as glass and plastic, is also provided by treatment with a coating of an epoxy resin. (see column 12, lines 5-15)".

(Office Action, pages 7-8). Applicants respectfully disagree.

As discussed above, Mandecki in view of Akram *et al.* does not teach a method for producing a labeled gene or protein, comprising binding the gene or protein to an LSI that comprises more than 320 million bits of memory. The teachings of Stavrianopoulos *et al.* do not cure the deficiencies of Mandecki and Akram *et al.* Stavrianopoulos *et al.* simply teach a method for using a probe that has been labeled with an enzyme or such to quantitatively detect target polynucleotide within a sample, and do not teach or suggest using "information" as a label. Stavrianopoulos *et al.* say nothing about the use of LSIs. Thus, even if the teachings of Mandecki, Akram *et al.*, and Stavrianopoulos *et al.* were combined, one of ordinary skill in the art could not have arrived at the currently claimed method.

It is respectfully requested that the rejection of claim 4 over Mandecki in view of Akram *et al.* and further in view of Stavrianopoulos be withdrawn.

Claim 4 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nova *et al.* in view of Akram *et al.* and further in view of Stavrianopoulos *et al.* (Office Action, page 8). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Nova in view of Akram teach the limitations of claims 1, 3, 5 and 7 as discussed above.
>
> Nova teaches a variety of synthetic plastic matrices as substrates at column 17, but Nova does not teach the specific substrates of claim 4.
>
> Stavrianopoulos teaches attachment of nucleic acids to plastic matrices (see column 12, lines 5-15, for example).
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the epoxy resin of Stavrianopoulos to attach the nucleic acids or proteins of Nova in view of Akram since Stavrianopoulos notes "An improved capability for fixing or immobilization of DNA to non-porous siliceous solid supports, such as glass and plastic, is also provided by treatment with a coating of an epoxy resin. (see column 12, lines 5-15)".

(Office Action, page 8). Applicants respectfully disagree.

As discussed above, Nova *et al.* in view of Akram *et al.* does not teach a method for producing a labeled gene or protein, comprising binding the gene or protein to an LSI that comprises more than 320 million bits of memory. The teachings of Stavrianopoulos *et al.* do not cure the deficiencies of Nova *et al.* and Akram *et al.* Stavrianopoulos *et al.* simply teach a method for using a probe that has been labeled with an enzyme or such to quantitatively detect target polynucleotide within a sample, and do not teach or suggest using "information" as a label. Stavrianopoulos *et al.* say nothing about the use of LSIs. Thus, even if the teachings of Nova *et al.*, Akram *et al.*, and Stavrianopoulos *et al.* were combined, one of ordinary skill in the art could not have arrived at the currently claimed method.

It is respectfully requested that the rejection of claim 4 over Nova *et al.* in view of Akram *et al.* and further in view of Stavrianopoulos be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Robert A. Schwartzman, Ph.D.
Attorney for Applicants
Registration No. 50,211

Date: July 11, 2007

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600
685408_1.DOC